Base Deficit as a Predictor of Mortality in Sepsis and Septic Shock

***Laxman Bhusal[1], Pratap Narayan Prasad[2], Yogendra Man Shakya[2], Ramesh Prasad Acharya[2]**

[1] DM Emergency Medicine Resident, Department of General Practice and Emergency Medicine, Tribhuvan University Teaching Hospital, Nepal.

[2] Professor, Department of General Practice and Emergency Medicine, Tribhuvan University Teaching Hospital, Nepal

ABSTRACT

Introduction: Sepsis is a common problem encountered in emergency room which needs to be intervened early. It is always difficult to have quick prognostic marker of sepsis in busy emergency. So this study was conducted to determine whether base deficit can be used as an indicator of mortality among septic patients in emergency room setup like ours.

Methods: It was a hospital based descriptive cross sectional study done at Tribhuvan University Teaching Hospital, Kathmandu from March 2018 to December 2018. Acute physiology and chronic health Evaluation II score (APACHE II), Base deficit, Sequential Organ Failure Assessment (SOFA) score on first day of arrival in emergency room was calculated. The association of 28-day outcome with acute physiology and chronic Health Evaluation II score, Base deficit value and SOFA score were derived.

Results: Out of 229 patients with septic shock 62 died (27%) and among 71 patients without septic shock, 12 died (16.9%).Overall mortality was 24.66 % (n= 74).The area under the ROC curve for Base deficit(0.864;95% C.I.=0.822-0.906), APACHE II (0.782; 95% C.I=0.718-0.848, SOFA (0.689;95% C.I=0.620-0.757) were greater than 0.7 except for SOFA which signifies these test to have fair efficacy to predict mortality.

Conclusions: High base deficit value predicts mortality in patients with sepsis and septic shock. The base deficit could be used as an alternate marker to predict mortality in septic patient. We recommend for large multicenter study with randomization so that the findings can be applied to general population and of different geographical situations.

Keywords: Base Deficit; Sepsis; Septic Shock, Predictor, Mortality

***Corresponding Author:**

Dr. Laxman Bhusal

Contact: bhusal.laxman@gmail.com, +977-9847185378

Access this article online

Quick Response Code

View PDF

Website: www.jkahs.org.np

DOI: http://doi.org/10.3126/jkahs.v2i2.25166

Article Info.

How to cite this article?

Bhusal L, Prasad PN, Shakya YM, Acharya RP. Base Deficit as a Predictor of Mortality in Sepsis and Septic Shock. Journal of Karnali Academy of Health Sciences. 2019;2(2): 81-88.

Received: 3 June, Accepted: 13 July, Published: 30 August 2019

Conflict of Interest: None, Source of Support: None

INTRODUCTION

Sepsis is one of the commonest presentations in emergency room with high mortality rate.[1] It has been called one of the oldest and most elusive syndrome in medicine. The most effort in sepsis has been given by Surviving Sepsis Campaign (SSC) guidelines which undoubtedly improved the process of care and outcome in the past decade.[2] One of the important way to decrease the mortality is early identification of sepsis and start early management.[3-5]

Base deficit is one of the important parameter in sepsis and septic shock investigation and management in current days.[6] If we can predict the mortality of patients with sepsis in emergency room and aggressively resuscitate them, the mortality rate can be decreased. In recent days base deficit is being investigated for its prognostic value in septic patients.[7] Base deficit is assumed to be the first accurate index of the non-respiratory component of acid base balance. Therefore base deficit value can provide a prognostic index that correlates with infection and easily available test in emergency room. The aim of this study is to determine whether the base deficit can be used in septic patients in our emergency set up to predict mortality.

METHODS

This hospital based, descriptive cross sectional study was conducted at Department of General Practice and emergency medicine, Tribhuvan University Teaching Hospital (TUTH) Nepal, From March 2018 to December 2018. Written consent was obtained from participants or from legal guardian when patients are too sick. Patient of greater than 18 years presented in TUTH emergency with diagnosis of sepsis were included. SOFA score of more than two was used to diagnose sepsis. Patients with an age less than 18 years, do-not-resuscitate order, pregnancy, left against the medical advice, were excluded. For each patient, at emergency vital signs were recorded with conscious level, temperature, heart rate,respiratory rate and systemic blood pressure. Laboratory parameters viz. haematocrit, blood glucose, total leucocyte count, serum sodium, serum potassium, serum creatinine and platelets count; were recorded. Patient arterial blood gas report was recorded with arterial pH, serum bicarbonate, Fi02, serum lactate and base deficit.

Sample size was calculated by $\mathbf{N = z^2pq/d^2}$ with Applying the sample size calculation formula based on hypothesis testing for two means from mortality of 59.6 % in sameer et al, and from article published in Scientific Reports in 2017, November with 14 % mortality where z = 1.96 at 95% confidence level, p = 86.7% p = percent area under the curve, q = 100-p = 13.3%, d = allowable error = 5% of p = 4.3. So, calculating by using above formula, the sample size of this study (n) is 300.

Descriptive statistics of demographic and laboratory variable were calculated with mean and percentages. Receiver operating characteristics (ROC) curve and Area under the receiver operating characteristics curve was used to evaluate the efficiency of base deficit in comparison to APACHE II and SOFA score; in predicting mortality within 28 days of hospital admission.

RESULTS

The age range of participants were 18 years to 101 years and mean age of 49.6 +/_ 18.25years in survival groups and 60.6 +/_ 17.26 years in mortality group. The overall mortality in septic patient was 24.7% (n=74) and the mortality in sepsis only was 16% and septic shock was 27%.There is increase in mortality rate as age increases with highest mortality of 54 % in age group of more than 77 years and minimum of 11 % in age group of 18-37 years(Fig 2).Most of the patients lie in severe base deficit(≥15) group (42.6%) followed by moderately high base deficit(-11 to-15) group(25%) and mild base deficit (≤ -10) group(32.3 %) (Table 3).Mean base deficit was -12.15+/_ 5.19 in survival group and -19.42+/_ 3.93 in mortality group.

In correlating between APACHE II score and base deficit ratio (Figure 1) shows positive deflection with correlation coefficient of 0.45 indicating that base deficit shows good mortality prediction.

The area under the ROC curve for base deficit (0.864;95% C.I = 0.822-0.906), APACHE II (0.782;95% C.I = 0.718-0.848), SOFA (0.689;95% C.I = 0.620-0.757) were greater than 0.7 except for SOFA score which signifies these score to be fair test to predict mortality among septic patients (Table 1). As base deficit has highest area under the curve among other prediction scores, it is the superior to other scores to predict mortality among septic patients. Bivariate logistic regression analysis was done to analyse effect of confounding factors like age, sex, presence of septic shock on mortality. Patients were further divided into two groups sepsis and septic shock. Out of 229 patients with septic shock 62 died (27%) and among 71 patients without septic shock, 12 died (16.9%).(Table 4).Overall mortality was 24.66 % (n=74).

Base deficit subgroups analysis showed 8% mortality in moderate base deficit group (-11 to-15) and 52 % in severe base deficit group (>-15) (Table 3).This shows increase trend of mortality with increase in base deficit value and vice versa.

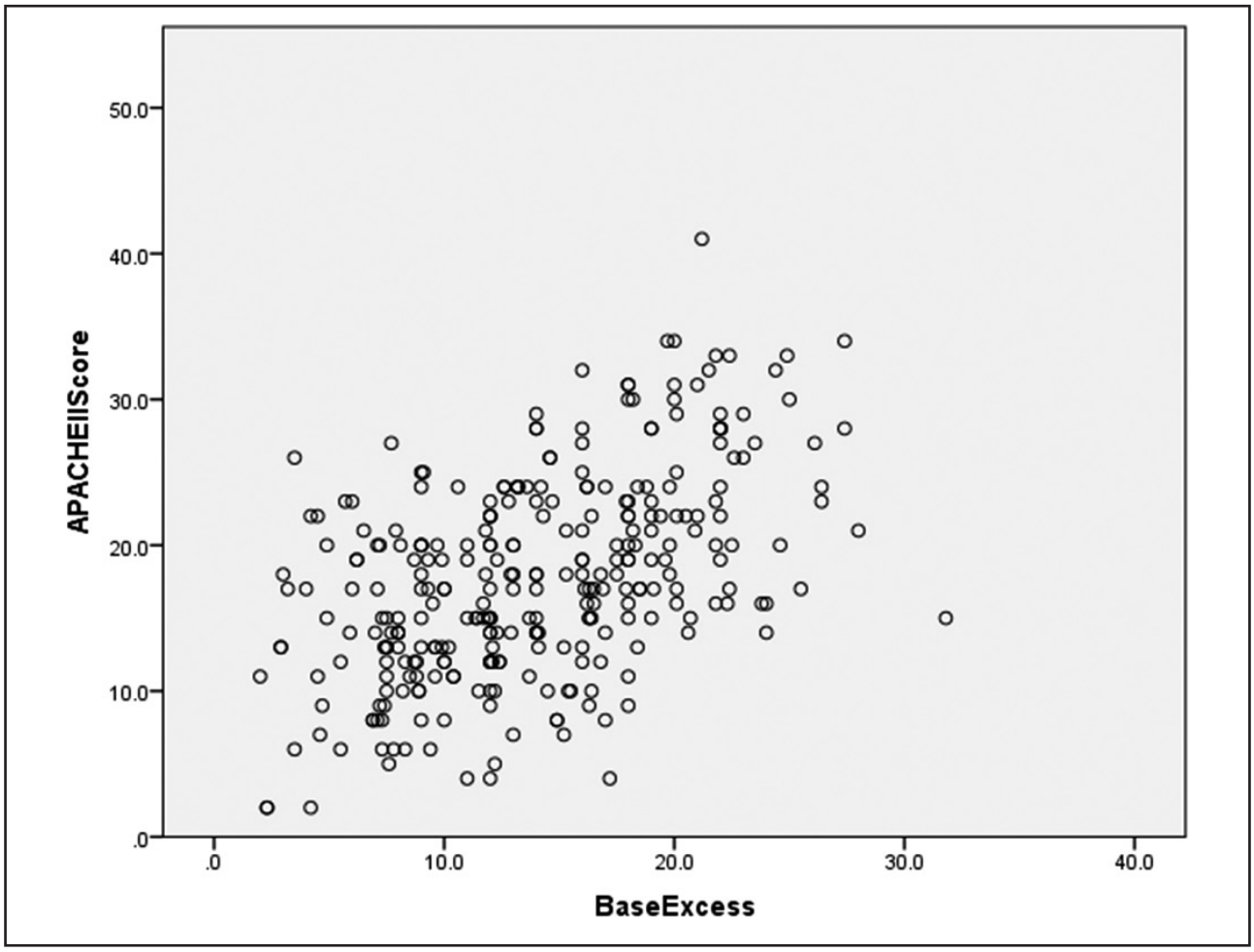

Figure 1: Relationship between base deficit and APACHE II score

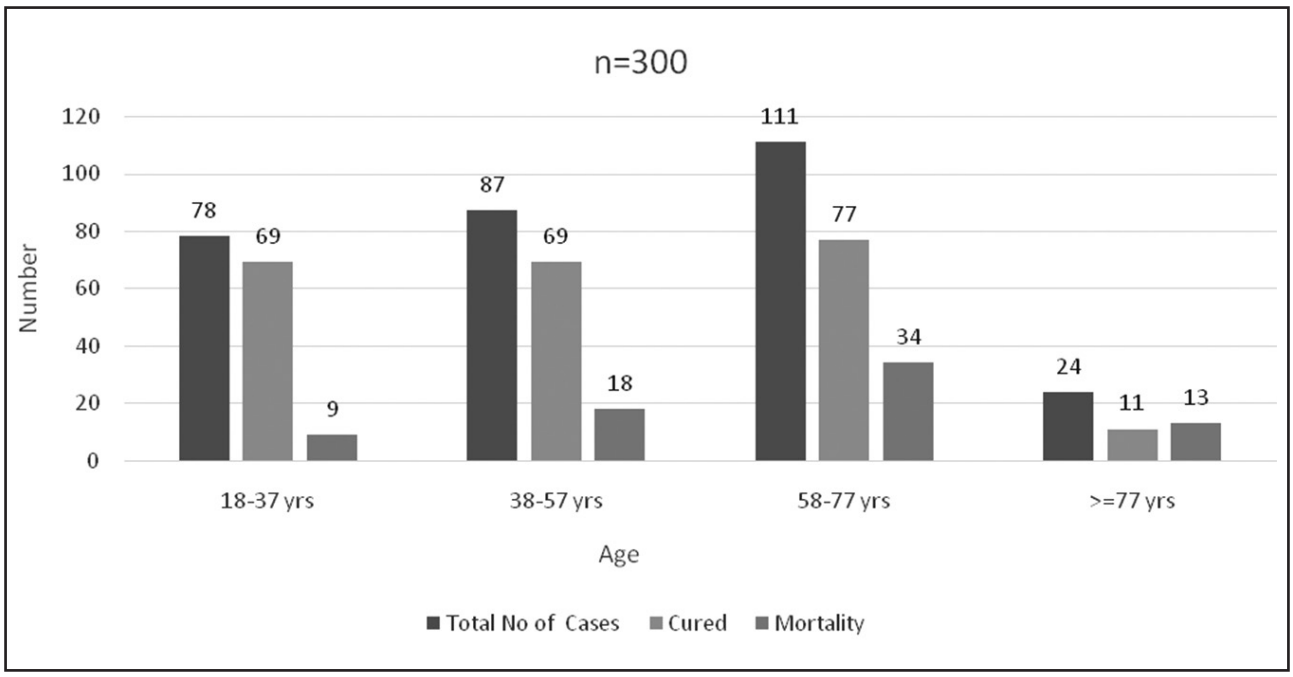

Figure 2: Outcome of septic patient in 28th day follow-up as per age group

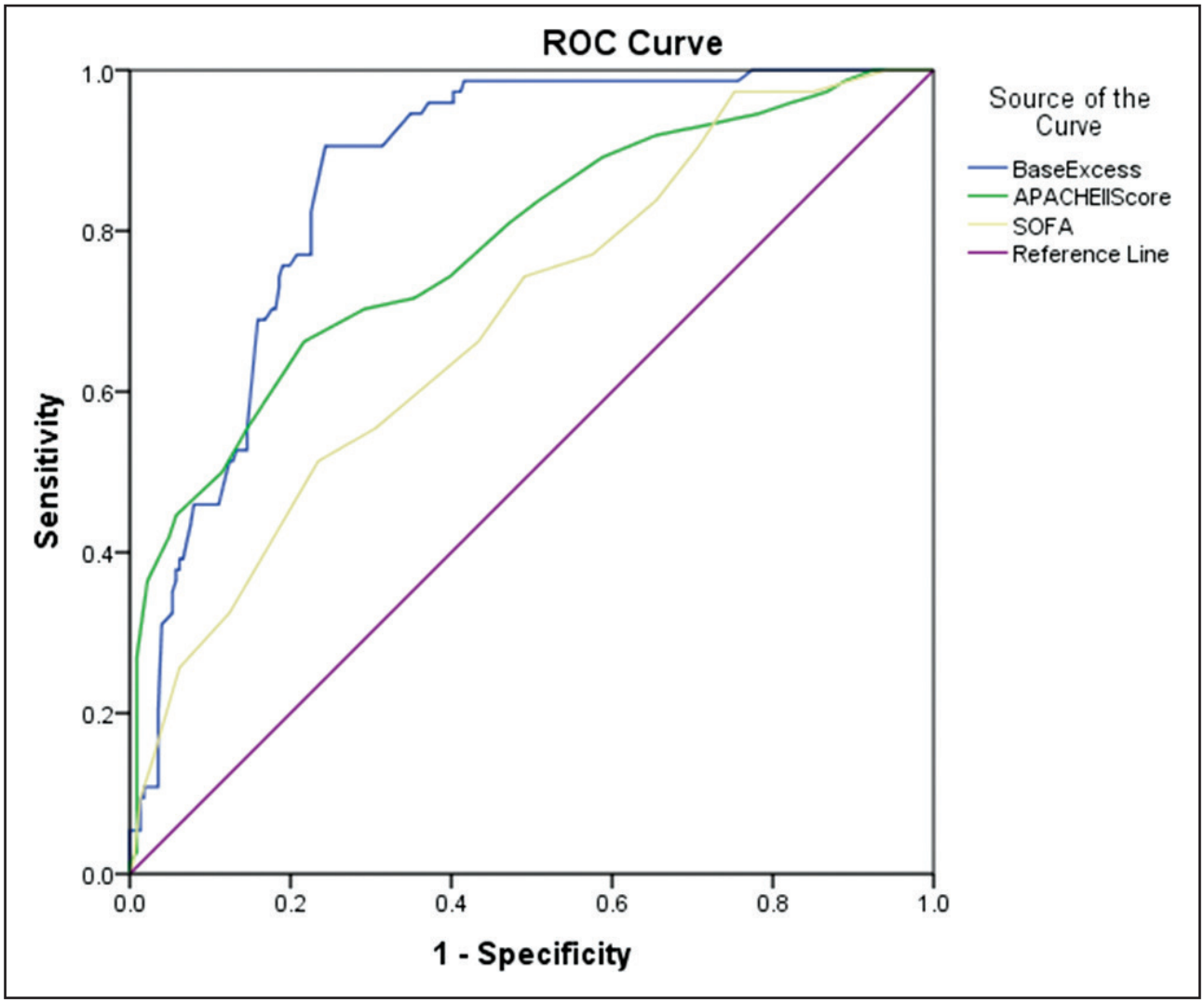

Figure 3: Receiver Operating characteristics curve analysis for base deficit, SOFA and APACHE II score to predict mortality in sepsis

Table 1: Area under the curve

Test Result Variable(s)	Area	95% Confidence Interval	
		Lower Bound	Upper Bound
Base Deficit	.864	.822	.906
APACHEII Score	.782	.718	.845
SOFA	.689	.620	.757

Table 2: Sensitivity, specificity, positive likelihood ratio and negative likelihood ratio for base deficit to predict mortality in sepsis

Base Deficit	Sensitivity	PLR	Specificity	NLR
-5.2	1.00	1.09	0.08	0.00
-10.1	0.99	1.66	0.41	0.03
-15.05	0.91	3.35	0.73	0.13
-18.1	0.55	3.79	0.85	0.52

Table 3: Binary logistic regression of base deficit subgroup and outcome

Base Deficit Classification	Cured (N = 226)			Mortality (N = 74)			95% Confidence interval	
	n	Row %	Column %	n	Row %	Column %	Lower	Upper
Low <5	4	100%	1.76%	0	0.0%	0.0%	0.000	0.000
Mild 5-10	92	98.9%	40%	1	1.07%	1.3%	0.000	0.000
Moderate 11-15	69	92%	30%	6	8%	8.1 %	0.001	0.073
Severe >15	61	47%	26%	67	52%	90%	0.032	0.195

Table 4: Bivariate logistic regression analysis of confounding factors and prognostic predictive scores

	Outcome Improved/Cured (N = 226)			Mortality (N = 74)			95% Confidence Interval	
	Mean	Row %	n	Mean	Row %	n	Lower	Upper
Age	49.64	75.3%	226	60.68	24.7%	74	1.019	1.051
Base Excess	-12.1	75.3%	226	-19.4	24.7%	74	1.243	1.443
APACHE II	16.61	75.3%	226	23.32	24.7%	74	1.139	1.261
SOFA	8.16	75.3%	226	10.75	24.7%	74	1.121	1.313
Chloride	103.9	75.3%	226	105.7	24.7%	74	1.103	1.235
Sex: Male		71%	116		28.8%	47	0.353	1.040
Female		80%	119		19.7%	27		
Septic Yes		72.9%	167		27%	62	0.919	3.624
Shock No		83.1%	59		16.9%	12		

DISCUSSION

With the early resuscitation and hour bundle care in the management; which decreases mortality in sepsis and septic shock, the focus has now moved to predicting mortality in septic patients. Our study showed that in the patients with sepsis and septic shock base deficit level obtained at admission in the emergency room can be used as an independent predictor of 28 day mortality. Lots of study have been done to investigate the biomarkers to predict mortality in sepsis[8] but only few studies have evaluate the prognostic significance of base deficit level in a septic patient. In-hospital mortality in our study was 24.7% which is nearly equal to study done by Cohen J et al with mortality of 25-30%.[9] With our study mortality in younger age group was 11% in 18-37 years group compared to 54% in old age group above 77 years whereas study done by Nasa P et al showed mortality of 45.6% (n=387) in younger age group as compared to 60.7% in old age group and 78.9% in very old age group.[10] So sepsis is significant burden on society and disproportionally affects the older adults and more than 60% of sepsis diagnosis are made in adults aged more than 65 years which is similar finding to our study.

Base deficit is assumed to be the first accurate index of the non-respiratory component of acid-base balance.[11] It is defined as the amount of strong acid that must be added to each litre of fully oxygenated blood to return the pH to 7.40 at a temperature of 37 degree centigrade and pCO_2 of 40 mmHg.[12, 13] The measurement of single lactate value in emergency room has several limitation, like in trauma, diabetic ketoacidosis, liver dysfunction level of lactate is high.[14] So base excess value is more important as it isn't much influenced by above factors and gives the proper interpretation value in metabolic acidosis in septic patients. In our study overall mortality till 28th day follow up was 74 (24.7%) and 27% with septic shock. It shows that one in every four patient diagnosed as sepsis or septic shock are dying, similar results were found in study done by Harm-Jan with 65 septic shock RCTs in 2018.[15]

APACHE II and SOFA scoring system were used widely to assess outcome in septic patient[16-18] but this is time consuming and difficult to assess immediately in busy emergency room situation. So we used base deficit as a marker of outcome in sepsis. It is found that increase in base deficit increases mortality in septic patients.[19, 20] Our study finding were similar with study done by Min Ho Seo in 2016 with hypoalbuminemia, low base excess value and tachypnoea to predict 28 day mortality in severe sepsis and septic shock patient in emergency department, which found that mortality in patients with sepsis and septic shock correlates with increased base excess level. It is found that base excess has slight higher area of under the ROC curve (AUROC=0.864) in comparison with APACHE II (AUROC = 0.782) which corelates with the above study done by Min Ho Seo. Study done by Min Ho Seo showed the AUC of the APACHE II score to be 0.6177(95% CI,0.5423-0.6931) 12whereas albumin, base deficit and respiratoryrate combined had AUC of 0.8173(95% CI,0.7605-0.8741) and conclude that, base excess can be chosen for predicting mortality then APACHE II. Our study had mean APACHE of 16 (S.D = 5.92) in survival group and 23.3 (S.D = 6.94) in mortality group , while study done by Sundaramoorty et al had mean APACHE of 24.3 in survival group with S.D of 6.48 and 32.39 in mortality group with S.D of 5.09.[21]

Limitation of Study: Sensitivity analysis of all confounders that could cause increase mortality in sepsis was not perform. Patients were generalized once they come to emergency room in spite of their level of treatment outside the hospital. It was a single center non-randomized study which has chances of biasness.

CONCLUSION

High base deficit value predicts mortality in patients with sepsis and septic shock. The base deficit could be used as an alternate marker to predict mortality in septic patient. We recommend for large multicenter

study with randomization so that the findings can be applied to general population and of different geographical situations.

ACKNOWLEDGEMENTS

I want to express special thanks to Dr. Pratap Narayan Prasad, Dr. Yogendra Man Shakya, Dr. Ramesh Prasad Acharya and special thank to all those patient who allow me to participate them in the study.

REFERENCES

1. Fleischmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P, et al. Assessment of Global Incidence and Mortality of Hospital-treated Sepsis. Current Estimates and Limitations. Am J Respir Crit Care Med. 2016;193(3):259-72.
2. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017;43(3):304-77.
3. Masyuk M WB, Lichtenauer M, Franz M, Kabich B, Muessig JM, Zimmermann G, Lauten A, Schulze C, Hoppe UC, Kelm M, Bakker J, Junc C. Prognostic relevance of serum lactate kinetics in critically ill patients. Intensive care medicine. 2018.
4. Shankar harim pG, Levy ML et al. Developing a new defination and assessing new clinical criteria for septic shock for the third internation consensus defination for sepsis and septic shock (sepsis-3). Journal of American Medical Association. 2016;315:775-87.
5. Lichtenauer M, Wernly B, Ohnewein B, Franz M, Kabisch B, Muessig J, et al. The Lactate/ Albumin Ratio: A Valuable Tool for Risk Stratification in Septic Patients Admitted to ICU. International journal of molecular sciences. 2017;18(9).
6. A K. Systematic bias in meta-analysis of time to antimicrobial in sepsis studies. Crit Care Med 2016;234-235.
7. Smith I, Kumar P, Molloy S, Rhodes A, Newman PJ, Grounds RM, et al. Base excess and lactate as prognostic indicators for patients admitted to intensive care. Intensive Care Med. 2001;27(1):74-83.
8. Jones AE SK, Kline JA. Performance of the mortality in Emergency Department sepsis score for predicting hospital mortality among patient with severe sepsis and septic shock. Am J Emerg Med. 2008;26:689-92.
9. Cohen J VJ, Adhikari NK, MAchd FA, Angus D, Calandra J, Jatan K, Glulien S, Delaloye J, Opal S et al. Sepsis a Road map for future research. Lancet infect Dis. 2015;15:581-614.
10. Nasa P JD, Singh U, Dang R, Arura V. Severe sepsis and its impact on outcome in elderly and very elderly patients admitted in intensive care unit. journal of intensive care medicine. 2012;27(3):179-8.
11. Min Ho Seo MC, Je sung you, hye sun lee, jung hwahong. hypoalbuminemia, low base excess value and tachypnea predict 28 day mortality in severe sepsis and septic shock patients in the emergency department. Yonse medical journal. 2016:1361-9.
12. Skellett S, Mayer A, Durward A, Tibby SM, Murdoch IA. Chasing the base deficit: hyperchloraemic acidosis following 0.9% saline fluid resuscitation. Archives of disease in childhood. 2000;83(6):514-6.
13. Morgan TJ, Clark C, Endre ZH. Accuracy of base excess-an in vitro evaluation of the Van Slyke equation. Crit Care Med. 2000;28(8):2932-6.
14. James JH, Luchette FA, McCarter FD, Fischer JE. Lactate is an unreliable indicator of tissue hypoxia in injury or sepsis. Lancet. 1999;354(9177):505-8.
15. Harm-Jan de Grooth Jp, Stephan A loer, Jean Jacques parienti, Heleen M. Unexplained mortality differences between septic shock trials:a systematic analysis of population characteristics and control group mortality rates. Intensive care Med. 2018;44:311-22.

16. Desai S, Lakhani JD. Utility of SOFA and APACHE II score in sepsis in rural set up MICU. The Journal of the Association of Physicians of India. 2013;61(9):608-11.

17. Raith EP, Udy AA, Bailey M, McGloughlin S, MacIsaac C, Bellomo R, et al. Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care UnitPrognostic Accuracy of SIRS Criteria and SOFA and qSOFA Scores Among ICU Patients With Suspected InfectionPrognostic Accuracy of SIRS Criteria and SOFA and qSOFA Scores Among ICU Patients With Suspected Infection. JAMA. 2017;317(3):290-300.

18. Lie KC, Lau CY, Van Vinh Chau N, West TE, Limmathurotsakul D. Utility of SOFA score, management and outcomes of sepsis in Southeast Asia: a multinational multicenter prospective observational study. 2018;6:9.

19. Montassier E, Batard E, Segard J, Hardouin JB, Martinage A, Le Conte P, et al. Base excess is an accurate predictor of elevated lactate in ED septic patients. Am J Emerg Med. 2012;30(1):184-7.

20. Park M, Azevedo LC, Maciel AT, Pizzo VR, Noritomi DT, da Cruz Neto LM. Evolutive standard base excess and serum lactate level in severe sepsis and septic shock patients resuscitated with early goal-directed therapy: still outcome markers? Clinics (Sao Paulo, Brazil). 2006;61(1):47-52.

21. VijayGanapathy S, Karthikeyan VS, Sreenivas J, Mallya A, Keshavamurthy R. validation of APACHE II scoring system at 24 hours after admission as a prognostic tool in urosepsis: A prospective observational study. Investigative and clinical urology. 2017;58(6):453-9.